IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF ARKANSAS

MARILYN STUBE and
THOMAS STUBE **PLAINTIFFS**

v. **NO. 6:19-CV-06087-SOH**

PFIZER INC. **DEFENDANT**

BRIEF IN SUPPORT OF MOTION TO DISMISS

Defendant Pfizer Inc. ("Pfizer") respectfully submits this Memorandum in Support of its Motion to Dismiss all causes of action asserted in Plaintiffs' Complaint pursuant to Federal Rules of Civil Procedure 12(b)(6) and 9(b). For the reasons discussed herein, Pfizer requests that Plaintiffs' Complaint be dismissed in its entirety and with prejudice.

INTRODUCTION

Plaintiffs Marilyn and Thomas Stube, both Arkansas residents, bring this product liability action alleging that they sustained injuries in connection with Mrs. Stube's use of Xeljanz (tofacitinib) to treat her rheumatoid arthritis. In November 2012, the Food and Drug Administration ("FDA") first approved Xeljanz, a breakthrough medication manufactured by Pfizer, as the first oral medication for the treatment of adult patients with moderately to severely active rheumatoid arthritis who had an inadequate response or intolerance to methotrexate. *See* Dkt. No. 2, ¶ 16. Prior to Xeljanz's approval, prescription treatment for rheumatoid arthritis was administered by injection or intravenous infusion. FDA also has approved Xeljanz for the treatment of patients with active psoriatic arthritis and moderately to severely active ulcerative colitis. *See id.*, ¶ 5 n.1; *id.*, ¶ 16 n.10.

Plaintiffs allege that Mrs. Stube began taking Xeljanz for her rheumatoid arthritis in March 2013. *Id.*, ¶ 11. Four years later, in March 2017, Mrs. Stube presented at an Arkansas

hospital with shoulder pain after moving a kayak. *Id*., ¶ 12. Four days later, she returned, complaining of chronic pain, fever, nausea, vomiting and shortness of breath, at which time she stopped taking Xeljanz. *Id.* Plaintiffs allege that the next day, Mrs. Stube experienced septic shock due to a Streptococcus Group A infection—an infection the hospital apparently did not diagnose at first—which ultimately led to multi-organ failure, gangrene, and amputation of all four of her limbs. *Id*., ¶¶ 5, 12–15.

Plaintiffs allege six causes of action, all of which are based on allegations that Pfizer failed to warn of the risk of "sepsis, amputation and increased risk of infection to females and the elderly" associated with Xeljanz use. *Id*., ¶ 37; *see also id*., ¶¶ 6, 33, 52, 57, 85(e). The causes of action include: (1) strict products liability/failure to warn; (2) fraud and fraudulent inducement; (3) breach of implied warranty; (4) negligence; (5) negligent misrepresentation; and (6) gross negligence. Plaintiffs also seek punitive damages. For the reasons discussed below, each cause of action fails as a matter of law.

First, the Xeljanz label adequately warned of the injury Mrs. Stube suffered. Since the very first day FDA approved Xeljanz, and throughout the entire four years that Mrs. Stube allegedly took the product, the label contained a boxed warning—FDA's most serious warning—which stated: "**Patients treated with XELJANZ are at increased risk for developing serious infections that may lead to hospitalization or death.**" *See* Exhibit A (Xeljanz label), at 2 (emphasis in original); *see also id*. at 1 (noting in the "Highlights of Prescribing Information" that "**[s]erious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving XELJANZ**" (emphasis in original)).[1] In addition, the Warnings &

[1] The Xeljanz label and all other FDA documents referenced herein are available on the FDA website at https://www.accessdata.fda.gov/scripts/cder/daf/#apphist. Pfizer requests that this Court take judicial notice of

Precautions section references specifically both infection and sepsis: "**Patients should be closely monitored for the development of signs and symptoms of infection** during and after treatment with XELJANZ. **XELJANZ should be interrupted if a patient develops a serious infection, an opportunistic infection, or sepsis**." *Id*. at 5 (emphasis added). Unfortunately, that is allegedly what happened to Mrs. Stube: she happened to develop a serious infection while taking Xeljanz that led to hospitalization and other serious consequences (though, thankfully, not her death).

Recognizing this barrier to their claims, Plaintiffs argue that the labeling defect relates not to the boxed warning of serious infections, but instead to the known ***consequences*** of serious infection, including sepsis, gangrene, and amputation, *see* Dkt. No. 2, ¶ 22 n.15—even though those were the events caused by Mrs. Stube's infection, about which the Xeljanz label warned. Indeed, it is well-known in the medical community that sepsis is one of several ways serious infections can lead to hospitalization or death. *See, e.g.*, CDC, What Is Sepsis?, https://www.cdc.gov/sepsis/what-is-sepsis.html (last visited Sept. 9, 2019) ("Sepsis is the body's extreme response to an infection. It is a life-threatening medical emergency. Sepsis happens when an infection you already have —in your skin, lungs, urinary tract, or somewhere else—triggers a chain reaction throughout your body. . . . When germs get into a person's body, they can cause an infection. If that infection isn't stopped, it can cause sepsis.").[2] And a label that

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these documents for purposes of this motion. *See Stahl v. United States Dept. Agric.*, 327 F.3d 697, 700 (8th Cir. 2003) ("The district court may take judicial notice of public records and may thus consider them on a motion to dismiss."); *see also Giddings v. Cradduck*, No. 5:16-cv-05035, 2017 WL 2791345, at *6-7 n.4, 5 (W.D. Ark. Jun. 6, 2017), report and recommendation adopted, 2017 WL 2799297 (W.D. Ark. Jun. 27, 2017) (taking judicial notice of the Mayo Clinic and the National Institute of Health's websites).

[2] A number of major medical institutions similarly note that sepsis is a known consequence of infection. *See, e.g.*, Mayo Clinic, https://www.mayoclinic.org/diseases-conditions/sepsis/symptoms-causes/syc-20351214 (last visited Sept. 9, 2019) ("Sepsis is caused by infection and can happen to anyone"); University of Michigan, https://healthblog.uofmhealth.org/health-topics/what-are-septic-shock-and-sepsis-facts-behind-these-deadly-conditions (last visited Sept. 9, 2019) ("Sepsis can result from any type of infection"); Cleveland Clinic,

warns of the ***cause*** (infection) and the ultimate ***consequences*** of an injury (hospitalization and potentially death) is not inadequate simply because it does not outline all possible paths between that cause and consequence. *See Estate of LaMontagne v. Bristol-Myers Squibb*, 111 P.3d 857 (Wash. Ct. App. 2005) (granting summary judgment for manufacturer and concluding that label warning on lactic acidosis and the possibility of death "unequivocally warned doctors of the risks and were adequate as a matter of law" where the plaintiff experienced lactic acidosis and eventually died of sepsis). Indeed, providing extraneous details of every intermediate, known stage of a condition in a label would contravene the very objective of the label to provide information in a clear and concise way so that a physician can make an informed prescribing decision. *See Guevara v. Dorsey Labs., Div. of Sandoz, Inc.*, 845 F.2d 364, 367 (1st Cir. 1998) (reviewing the adequacy of the warning "measured against the general level of knowledge existent in the target community," and concluding that label warning on allergic reactions was adequate where the plaintiff experienced a skin rash and alleged she was not warned of the specific kind of reaction she experienced). As a result, the Xeljanz label adequately warned of the injury Mrs. Stube experienced, and Plaintiffs' entire Complaint should be dismissed.

Second, federal law preempts Plaintiffs' challenge to the adequacy of the Xeljanz label. Under federal regulations, as Plaintiffs implicitly concede in their Complaint, *see* Dkt. No. 2, ¶ 22 n.15, a manufacturer cannot unilaterally change an FDA-approved boxed warning, like the one included in Xeljanz labeling relating to serious infections at the time Mrs. Stube was prescribed Xeljanz. *See* 44 Fed. Reg. 37,434, 37,448 (Jun. 26, 1979). Because it was impossible for Pfizer to change the Xeljanz boxed warning under federal law to provide the warnings Plaintiffs claim were required by state law, impossibility preemption applies and Plaintiffs'

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https://my.clevelandclinic.org/health/diseases/12361-sepsis (last visited Sept. 9, 2019) ("Bacterial infections are the most common cause of sepsis"); University of Pittsburgh Medical Center, https://share.upmc.com/2017/09/what-is-sepsis/ (last visited Sept. 9, 2019) ("Any infection in your body can lead to sepsis…").

claims should be dismissed. With respect to changes to other portions of the label, Plaintiffs fail to allege any "newly acquired information," which would have been necessary for Pfizer to make any unilateral change. *See* 21 C.F.R. § 314.70(c)(6)(iii)(A). Absent any allegations that Pfizer had "newly acquired information" that revealed risks of a different type or greater severity or frequency than previously included in submissions to FDA and warned of in the Xeljanz label, federal law preempts any claim based on the adequacy of Xeljanz's warnings. *See Utts v. Bristol-Myers Squibb Co.*, 226 F. Supp. 3d 166, 182 (S.D.N.Y. 2016) ("*Utts I*"); *see also Gibbons v. Bristol-Myers Squibb Co.*, 919 F.3d 699, 708-09 (2nd Cir. 2019).

Third, Arkansas law is well settled that pharmaceutical manufacturers do not have a duty to warn patients or the general public of the risks of prescription medications. Pfizer's duty to warn runs only to Mrs. Stube's physician, not to Mrs. Stube or the public. To the extent Plaintiffs' claims are based on a duty that does not exist, they are fatally deficient under the Arkansas learned intermediary doctrine. *Boehm v. Lilly & Co.*, No. 4:10-cv-159-DPM, 2012 WL 12848432, at *3 (E.D. Ark. Oct. 4, 2012), *aff'd*, 747 F.3d 501 (8th Cir. 2014) (citing *Hill v. Searle Labs.*, 884 F.2d 1064, 1070 (8th Cir. 1989) (applying Arkansas law)).

***Fourth*,** in addition to the above fatal flaws, Plaintiffs' fraud claim is not pled with the particularity required pursuant to Federal Rule of Civil Procedure 9(b). Fed. R. Civ. P. 9(b). Binding law obligates Plaintiffs to plead "'the time, place[,] and contents of false representations, as well as the identity of the person making the misrepresentation and what was obtained or given up thereby.'" *Schaller Tel. Co. v. Golden Sky Sys., Inc.*, 298 F.3d 736, 746 (8th Cir. 2002) (quoting *Bennett v. Berg*, 685 F.2d 1053, 1062 (8th Cir. 1982). The Complaint is bereft of such detail.

Fifth, Plaintiffs' negligent misrepresentation claim also fails under Rule 9(b), and also because Arkansas law does not recognize a cause of action for negligent misrepresentation. *See Owen v. Arthrex, Inc.*, No. 6:19-CV-6026, 2019 WL 2583519, at *2 (W.D. Ark. Jun. 24, 2019); *see also S. Cty., Inc. v. First W. Loan Co.*, 315 Ark. 722, 725, 871 S.W.2d 325, 326 (1994).

Sixth, Plaintiffs have not pled facts sufficient to support a claim for gross negligence. Plaintiffs' allegations in their gross negligence claim are indistinguishable from a claim for simple negligence, and therefore do not allege that Pfizer went well beyond merely negligent conduct and instead failed "to use even slight care." *See IPSCO Tubulars, Inc. v. Ajax TOCCO Magnathermic Corp.*, 779 F.3d 744, 752 (8th Cir. 2015).

Finally, Plaintiffs' request for punitive damages should be stricken. Negligence, even gross negligence, will not support an award of punitive damages under Arkansas law. *See Nat'l By-Products, Inc. v. Searcy House Moving Co.*, 292 Ark. 491, 494, 731 S.W.2d 194, 196 (1987). Here, however, the Complaint concedes that the Xeljanz label included the strongest possible warning about the very harm Mrs. Stube allegedly experienced. Plaintiffs' challenge to the specific contents of that label demonstrates nothing more than their disagreement with FDA's decision-making processes, and the Complaint includes no support for the allegation that Pfizer acted recklessly with respect to its communication of the relevant risks as required by federal law.

For these reasons, and as detailed more thoroughly below, Pfizer respectfully requests the Court dismiss Plaintiffs' Complaint in its entirety and with prejudice.

LEGAL STANDARD

In evaluating a motion to dismiss, federal courts follow the pleading requirements established by the Supreme Court in *Ashcroft v. Iqbal*, 556 U.S. 662 (2009), and *Bell Atlantic*

Corp. v. Twombly, 550 U.S. 544 (2007). "To survive a [Rule 12(b)(6)] motion to dismiss, a complaint must contain sufficient factual matter, accepted as true, to 'state a claim to relief that is plausible on its face.'" *Iqbal*, 556 U.S. at 678 (quoting *Twombly*, 550 U.S. at 570). Additionally, "[f]actual allegations must be enough to raise a right to relief above the speculative level[.]" *Twombly*, 550 U.S. at 555. This "plausibility standard" requires "more than an unadorned, the-defendant-unlawfully-harmed-me accusation." *Iqbal*, 556 U.S. at 678. "[A] plaintiff's obligation to provide the grounds of his entitle[ment] to relief requires more than labels and conclusions, and a formulaic recitation of the elements of a cause of action will not do[.]" *Twombly*, 550 U.S. at 555 (internal quotation marks and citations omitted). Although a plaintiff's allegations generally must be accepted as true, "[t]he plausibility standard requires more than simply the possibility that a defendant has acted unlawfully; it requires 'enough fact[s] to raise a reasonable expectation that discovery will reveal evidence of [the claim].'" *Trust v. Sunbeam Prods., Inc.*, Case No. 2:13-CV-02039, 2013 WL 12108955, at *1 (W.D. Ark. Apr. 18, 2013) (quoting *Twombly*, 550 U.S. at 556).

ARGUMENT

I. Plaintiffs' Entire Complaint Fails as a Matter of Law.

All of Plaintiffs' causes of action are based on allegations that Pfizer failed to warn of the risk of "sepsis, amputation and increased risk of infection to females and the elderly" associated with Xeljanz use. Dkt. No. 2, ¶ 37; *see also id.*, ¶¶ 6, 33, 52, 57, 85(e). Each claim fails as a matter of law for three independent reasons: (1) the Xeljanz label is adequate as a matter of law; (2) all of Plaintiffs' claims are preempted by federal law; and (3) each of Plaintiffs' claims is barred by the informed intermediary doctrine.

Plaintiffs do not challenge the adequacy of the boxed warning on the Xeljanz label regarding the risk of serious infections that can lead to hospitalization and even death. Instead, Plaintiffs challenge the level of specificity of the label relating to infections, and allege that, from the time of approval, the Xeljanz label has failed to warn of: (1) "the risk of sepsis" or that "cases of sepsis had occurred in clinical trials"; (2) "the risk of amputations"; (3) the "elevated risk of serious infection in individuals with pre-existing viral infections"; or (4) the "increased risks of sepsis and serious infections in the elderly and females." Dkt. No. 2, ¶ 21. In further support of their failure-to-warn claims, Plaintiffs contend that the label "recommends (to treating physicians, not prescribing physicians) 'interrupting' Xeljanz treatment in patients *after* they develop a 'serious infection, an opportunistic infection, or sepsis,'" which they claim is "not a sepsis warning for prescribing physicians." *Id*., ¶ 21 n.14 (emphasis in original). Plaintiffs also contend that the language in the FDA-approved label is "after-the-fact language" that "does not warn for or disclose the risk of sepsis *before* the patient starts the drug." *Id*. (emphasis in original).

These labeling criticisms are insufficient as a matter of law, for two reasons. First, a label is adequate under Arkansas law so long as it "puts a reasonably prudent physician on notice of a particular risk" of which a manufacturer has actual or constructive knowledge. *Bell v. Pliva, Inc.*, 845 F. Supp. 2d 967, 970 (E.D. Ark. 2012), *rev'd in part on other grounds*, *Bell v. Pfizer, Inc.*, 716 F.3d 1087 (8th Cir. 2013) (citing *In re Prempro Prods. Liab. Litig.*, 514 F.3d 825, 830 (8th Cir. 2008)). Here, the Xeljanz label put physicians on notice that patients taking Xeljanz are at an increased risk of serious infections and that such infections could lead to hospitalization, which is allegedly what happened to Mrs. Stube.

Second, Plaintiffs' failure-to-warn claims are preempted as Pfizer is not permitted to unilaterally change the boxed warning, and Plaintiffs have not identified any newly acquired information that would support Pfizer making any changes to the FDA-approved Xeljanz label. *See Pliva, Inc. v. Mensing*, 564 U.S. 604, 619-20 (2011); *Wyeth v. Levine*, 555 US 555, 574 (2009); 21 C.F.R. § 314.3(b).

A. The Warnings in the Xeljanz Label Are Adequate as a Matter of Law.

"Under Arkansas law, a drug warning is adequate so long as it puts a reasonably prudent physician on notice of a particular risk that the manufacturer has actual or constructive knowledge of at the time of distribution." *Bell*, 845 F. Supp. 2d at 970. Plaintiffs allege that Mrs. Stube was prescribed Xeljanz from 2013 until March 2017. Dkt. No. 2, ¶¶ 11-12. Plaintiffs' claims should be dismissed with prejudice because the Xeljanz label in effect when Mrs. Stube took the medication warned of the risks of serious infections in clear and unambiguous language, and was therefore adequate as a matter of law.

The Xeljanz label was approved for use by FDA in November 2012. *Id.*, ¶ 16. Since November 2012, there has always been a boxed warning—the strongest warning permitted under federal regulations—on the Xeljanz label for risk of serious infections: "**Patients treated with XELJANZ are at increased risk for developing serious infections that may lead to hospitalization or death.**" Exhibit A, at 2 (emphasis in original); *see also id.*, at 1 ("**Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving XELJANZ**.") (emphasis in original). Sepsis is a well-known, foreseeable potential consequence of a serious infection. *See, e.g.*, CDC, What Causes Sepsis?, https://www.cdc.gov/sepsis/what-is-sepsis.html (last visited Sept. 9, 2019) ("When germs get into a person's body, they can cause

an infection. If that infection isn't stopped, it can cause sepsis."); Exhibit B (Mayo Clinic website describing sepsis noting that "[s]epsis is a potentially life-threatening condition caused by the body's response to an infection" that can "cause blood clots to form in your organs and in your arms, legs, fingers and toes — leading to varying degrees of organ failure and tissue death (gangrene)").

Contorting their claims in an attempt to bypass the boxed warning, Plaintiffs instead point to additional language that appears in the "**WARNINGS AND PRECAUTIONS**" section of the label containing "**WARNINGS**" for "**SERIOUS INFECTIONS AND MALIGNANCY**." *See* Exhibit A, at 1, 5. That section of the Xeljanz label warns specifically that

> [p]atients should be *closely monitored* for the development of signs and symptoms of infection during and after treatment with XELJANZ. XELJANZ should be interrupted if a patient develops a serious infection, an opportunistic infection, or sepsis. A patient who develops a new infection during treatment with XELJANZ should undergo prompt and complete diagnostic testing appropriate for an immunocompromised patient; appropriate antimicrobial therapy should be initiated, and the patient should be closely monitored.

Id. at 5 (emphasis added). Contrary to Plaintiffs' position, this warning is directed to the *prescribing* physician *before* the prescription of Xeljanz. The label could not be clearer—the prescribing physician is to closely monitor the patient taking Xeljanz for "signs and symptoms of infection" and is instructed that "Xeljanz should be interrupted if a patient develops a serious infection, an opportunistic infection, or sepsis." Unfortunately, it appears Mrs. Stube was not closely monitored for signs of infection, her serious infection was initially missed, and she did not return to a hospital for treatment for four days. Dkt. No. 2, ¶ 12.

Additionally, throughout the time Mrs. Stube took Xeljanz, the label has cautioned: "As there is a higher incidence of infections in the elderly population in general, caution should be used when treating the elderly." *See* Exhibit A, at 14. Moreover, it is widely known in the

medical community that the elderly, people with chronic medical conditions, and people with weakened immune systems are at increased risk of sepsis from an infection. *See* CDC, Who is at risk?, https://www.cdc.gov/sepsis/what-is-sepsis.html?s_cid=NCEZID-Sepsis-501 (last visited Sept. 9, 2019).

Plaintiffs cite no population or study-based data to support their claim of an increased risk of serious infection in females, only anecdotal case reports of sepsis that happened to occur in female patients. *See* Dkt. No. 2, ¶ 22. However, adverse events are more likely to be reported in women with rheumatoid arthritis because rheumatoid arthritis is more prevalent in women than men in the general population (by a ratio of 3:1). *See* R. van Vollenhoven, "Sex Differences in Rheumatoid Arthritis: More than Meets the Eye." BMC Med. 2009;7:12. In fact, the only clinical trial study Plaintiffs cite as identifying the female gender as an "increased risk factor[] for serious infection"—the Cohen et al. (2017) study, *see* Dkt. No. 2, ¶ 22—shows a 20% *decreased* risk of serious infection in women compared to men taking Xeljanz. *See* Cohen, et al., "Long-term safety of tofacitinib for the treatment of rheumatoid arthritis up to 8.5 years: integrated analysis of data from global clinical trials." Ann Rheum Dis. 2017;76(7):1253-1262, at Figure 2, A.

Plaintiffs also point to the inclusion of sepsis in the Xeljanz label approved by other countries, as well as the inclusion of sepsis in a black box warning on the FDA-approved label of another rheumatoid arthritis drug, Enbrel, to argue that the Xeljanz label is inadequate. *See* Dkt. No. 2, ¶¶ 6, 9. However, prior to Xeljanz's approval, FDA reviewed the Xeljanz clinical trial data Pfizer submitted, which included adverse events of sepsis due to infection. *See* Exhibit C, FDA Medical Review, Clinical Review by Nikolay P. Nikolov, MD at 129, 258, https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/203214Orig1s000MedR.pdf (noting

sepsis AEs in Xeljanz clinical trials). Based on its review, FDA determined the precise content of the language in the label in effect at the time of approval, and Pfizer could not have changed that label absent newly acquired information. *See* section I.B *infra*. Moreover, in the time since Xeljanz was approved for rheumatoid arthritis, FDA has reviewed safety and efficacy data for Xeljanz several times in additional patient populations, approving new indications and reaffirming that the label adequately warned of serious infections and their foreseeable consequences. *See, e.g.*, Letter from FDA to Pfizer regarding Supplemental Approval, Dec. 14, 2017, https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2017/203214Orig1s017,208246ORig1s003ltr.pdf (last visited Sept. 9, 2019) (granting approval for treatment in adult patients with psoriatic arthritis); Letter from FDA to Pfizer regarding Supplemental Approval, May 30, 2018, https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/203214Orig1s018ltr.pdf (last visited Sept. 9, 2019) (granting approval for treatment in adult patients with ulcerative colitis).

Foreign regulatory decisions regarding whether or how to include sepsis in labels under those countries' standards are irrelevant in determining whether the U.S. label is adequate under U.S. legal standards. *See In re Baycol Prod. Litig.*, 532 F. Supp. 2d 1029, 1054 (D. Minn. 2007) (holding expert testimony regarding foreign regulatory actions was inadmissible); *see also In re Mirena IUD Prod. Liab. Litig.*, 169 F. Supp. 3d 396, 477 (S.D.N.Y. 2016) (noting that "[t]here is no reason to believe that the regulatory framework of Canada or Germany is similar to the FDA's system" and excluding expert testimony that summarized foreign regulatory history or "impl[ied] that an action required abroad was necessarily required in the U.S."); *McDowell v. Eli Lilly & Co.*, 13 Civ. 3786, 2015 WL 845720, at *5 (S.D.N.Y. Feb. 26, 2015) ("The mere existence of a differently structured and written European label does not establish that the U.S. label is

insufficient, misleading, or legally inadequate, nor is foreign regulatory action even appropriate as a subject of expert testimony in pharmaceutical cases."). Similarly, a declaration from Mrs. Stube's Texas-based rheumatologist opining on what he believes should be included in a label, in hindsight, based on the unfortunate experience of his patient, is not a proper substitute for FDA's judgment on the adequacy of the warnings in the Xeljanz label.

Because the Xeljanz label "puts a reasonably prudent physician on notice of" the risk the specific adverse event allegedly suffered by Mrs. Stube (serious infection) and the serious potential consequences of that event (hospitalization and even death), the warnings in the Xeljanz label are adequate as a matter of law. *Bell*, 845 F. Supp. 2d at 970. Accordingly, all of Plaintiffs' claims fail to state a claim upon which relief may be granted and should be dismissed.

B. Plaintiffs' Claims Are Preempted by Federal Law.

Plaintiffs' claims also should be dismissed with prejudice because they are preempted by federal law under the doctrine of impossibility preemption. The Supremacy Clause of the U.S. Constitution provides that federal law "shall be the supreme Law of the Land." U.S. Const., art. VI, cl. 2. Federal law impliedly preempts state law "where it is 'impossible for a private party to comply with both state and federal requirements.'" *Mutual Pharm. Co. v. Bartlett*, 570 U.S. 472, 480 (2013). Impossibility preemption exists where a private party could not "independently do under federal law what state law requires of it." *Mensing*, 564 U.S. at 620. "[W]hen a party cannot satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for pre-emption purposes." *Id*. at 623.

The Food, Drug, and Cosmetic Act of 1938 ("FDCA") regulates the manufacture and sale of prescription medications. *Merck KGAA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 196

(2005). Under the FDCA, in seeking approval to market a new medication, a sponsor must demonstrate that the medication is "safe and effective and that the proposed label is accurate and adequate" and provide FDA with preclinical and clinical information. *Mensing*, 564 U.S. at 612 (citing 21 U.S.C §§ 355(b)(1), (d)); *Wyeth*, 555 US at 567; *see also* 21 U.S.C §§ 355(i)(1)(A), (b)(1), (d); 21 C.F.R §§ 312.23(a)(5), (a)(8).

To grant initial market approval, FDA must determine, "based on a fair evaluation of all material facts," that the proposed label is not "false or misleading in any particular." 21 U.S.C § 355(d)(7); 21 C.F.R § 314.125 (b)(6). Accordingly, "FDA's premarket approval of a new drug application includes the approval of the exact text in the proposed label." *Wyeth*, 555 U.S. at 568; *see also* 21 U.S.C § 355(d); 21 C.F.R § 314.105(b). Once approved, a manufacturer is prohibited from marketing the medication with a label that differs from the exact text of the FDA-approved label. 21 U.S.C § 352(a), (f).

A manufacturer is also prohibited from making unilateral labeling changes (i.e., those made without FDA's prior approval), except as permitted by the "changes being effected" ("CBE") regulation. 21 CFR § 314.70(c)(6)(iii)(A). Under the CBE process, a manufacturer only may add or strengthen the label unilaterally (without waiting for FDA's approval) based on "newly acquired information." *Id.* "Newly acquired information" includes data, analyses, or other information not previously submitted to FDA, but only "if the studies, events, or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA." *Id.*, § 314.3(b). A plaintiff may avoid preemption only if "the complaint alleges a labeling deficiency that [the defendant manufacturer] could have corrected using the CBE regulation." *See In re Celexa & Lexapro Mktg. & Sales Pracs. Litig.*, 779 F.3d 34, 41 (1st Cir. 2015) (affirming dismissal of plaintiffs' claims on preemption grounds where the alleged

inadequacy of the label was not based on newly acquired information); *Gibbons*, 919 F.3d at 708-09 (affirming dismissal of plaintiffs' claims because "they consist of 'conclusory and vague' allegations and do not plausibly allege the existence of newly acquired information that could have justified Defendants' revising the [medication] label through the CBE regulation"); *see also Wyeth*, 555 U.S. at 574; *Bartlett*, 570 U.S. at 492; *Mensing*, 564 U.S. at 619-20; *Utts v. Bristol-Myers Squibb Co.*, 251 F. Supp. 3d 644, 672 (S.D.N.Y. 2017) ("*Utts II*"). Where a manufacturer cannot use the CBE process, and instead must seek FDA's prior approval before making a label change, any personal injury claim predicated on an allegation that the manufacturer should have changed the label is preempted. *See Gibbons*, 919 F.3d at 708; *In re Celexa*, 779 F.3d at 41; *Wyeth*, 555 U.S. at 574; *Bartlett*, 570 U.S. at 492; *Mensing*, 564 U.S. at 619-20; *see also Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1672, 203 L. Ed. 2d 822 (2019) (the question of preemption is one for a judge to decide, not a jury).

Here, Plaintiffs admit that Pfizer cannot unilaterally change a FDA-approved boxed warning on serious infections. *See* Dkt. No. 2, ¶ 22 n.15; *see also* 44 Fed. Reg. 37,434, 37,448 (Jun. 26, 1979). Such a change is not permitted through the CBE regulation. Instead, Plaintiffs contend that "Pfizer failed to fully and accurately report to the FDA and prescribing physicians . . . scientific literature regarding the Xeljanz-related frequency, incidence, and mortality rates related to sepsis, the risk of amputations, and subpopulations risks to the elderly and females." *See* Dkt. No. 2, ¶¶ 22–24. Plaintiffs allege that

> [s]pecifically, Plaintiffs' claims in this case are limited to i) pre- and post-approval claims relating to warnings that have never been in the Xeljanz label regarding the risk of sepsis, subpopulation risks to females and the specifically-identified serious adverse events associated with Xeljanz use (*e.g.*, multiorgan failure, soft tissue and skin infections, gangrene and amputations), and ii) post-approval claims relating to Pfizer's vastly understated Section 8 reference to an increased frequency of infections in the elderly and claims relating to herpes zoster on the basis that new safety information (addressed in the Complaint) has

> emerged since NDA approval. In fact, Pfizer changed its serious infection warning for the elderly population after Mrs. Stube was injured."

Id., at ¶ 22 n.15.

Plaintiffs' pre-approval claims are preempted in their entirety, because at the time of its approval, FDA approved the exact text of the Xeljanz label. *See In re Celexa*, 779 F.3d at 41; *Gibbons*, 919 F.3d at 708-09; *Wyeth*, 555 U.S. at 574; *Utts II*, 251 F. Supp. 3d at 672. With respect to post-approval claims, Plaintiffs point to no "newly acquired information" sufficient to support a CBE label change related to either serious bacterial infections of the type Mrs. Stube allegedly suffered or the resulting sepsis that occurred as a consequence of her infection. Plaintiffs cite no data, analyses, or other information that was not previously submitted to FDA or that "reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA." *See* 21 CFR § 314.3(b). The incidence rates that Plaintiffs cite for both serious infection with Xeljanz and for sepsis in the general population were available at the time of approval. The fact that the E.U.'s regulatory authorities chose to cite that rate in the E.U. label and FDA chose not to cite that particular rate in the U.S. label is irrelevant. And the post-approval scientific studies that Plaintiffs cite do not provide data that reveal a greater frequency or severity of serious infections or sepsis. Moreover, the incidence rate of sepsis of "up to 1 in 1,000" in the E.U. label, *see* Dkt. No. 2, ¶ 19, does not constitute information that reveals a "greater severity or frequency of sepsis" either. Indeed, it would be factually inappropriate to add this information to the U.S. label, as the incidence of sepsis in the United States is estimated at 3 cases per 1,000 in the general population. *See* Exhibit D (Angus et al., "Epidemiology of Severe Sepsis in the United States: Analysis of Incidence, Outcome, and Associated Costs of Care." Crit. Care Med. 2001;29:1303-10); *see also* Exhibit E (Martin et al., "The Epidemiology of Sepsis in the United States from 1979 through 2000." N. Eng. J. Med. 2003;348:1546-54).

Finally, the Xeljanz label at the time Mrs. Stube took Xeljanz contained a warning that: "As there is a higher incidence of infections in the elderly population in general, caution should be used when treating the elderly." *See* Exhibit A, at 14. Additional information added to the Xeljanz label regarding the herpes zoster virus (shingles) and vaccine, *see* Dkt. No. 2, ¶ 22 n.15, is in no way related to Mrs. Stube's sepsis due to Streptococcus Group A bacterial infection. Nor does this information reveal risks of a greater frequency or severity of serious infections in the elderly of the type Mrs. Stube suffered. *See id*., at ¶ 22. Thus, Plaintiffs have not identified any new information relevant to Plaintiffs' claims that would support a label change under the CBE process to the non-boxed warning portions of the Xeljanz label.

Because Pfizer would not have been able to change the Xeljanz label under federal law, it was impossible for Pfizer to provide the warnings Plaintiffs claim were required by state law. Accordingly, Plaintiffs' claims are preempted by federal law and should be dismissed.

C. The Learned Intermediary Doctrine Bars Plaintiffs' Claims.

"Under settled Arkansas law, the prescribing physician, not the consumer, is the person who must be warned of a drug's risks." *Boehm*, 2012 WL 12848432, at *3 (citing *Hill*, 884 F.2d at 1070 (applying Arkansas law)).

Although Pfizer's duty to warn extended only to Mrs. Stube's prescribing physician, the Complaint alleges that Pfizer failed to warn Plaintiffs and the public of the alleged risks associated with Xeljanz. *See, e.g.*, Dkt. No. 2, ¶¶ 21, 55, 85(e). All of Plaintiffs' claims predicated upon Pfizer's alleged duty to warn Plaintiffs or the public, rather than solely Mrs. Stube's prescribing physician, should be dismissed.

II. Plaintiffs Fail to State a Claim for Fraud.

In the Complaint, Plaintiffs attempt to state a cause of action for "fraud and fraudulent inducement." *See* Dkt. No. 2, ¶¶ 58–73. In doing so, Plaintiffs rely on various alleged "duties" owed under federal regulations and "to the medical community." *See, e.g.*, *id.*, ¶¶ 59–62. Pfizer, according to the Complaint, allegedly breached those duties by failing to disclose certain risks associated with Xeljanz use. *See id.*, ¶ 64. Plaintiffs also allege that Pfizer "deliberately and intentionally misrepresented to, and omitted and/or concealed material facts from, consumers, including Plaintiffs, and [Mrs. Stube's] prescribing physician, that [Pfizer's] product Xeljanz was safe when used as intended." *Id.*, ¶ 66. Though Plaintiffs do not identify the individual who made those "misrepresentations," the specific dates on which the "misrepresentations" were made, or the specific contents of the "misrepresentations," they nonetheless maintain that Mrs. Stube acted "[i]n reliance upon [Pfizer's] misrepresentations (and the absence of disclosure of the serious health risks)," in taking Xeljanz. *Id.*, ¶ 70.

Plaintiffs' fraud-based claims are insufficiently pleaded under Rule 9(b). The applicable standard is settled law in this Circuit, as Plaintiffs are required to allege "'the time, place[,] and contents of false representations, as well as the identity of the person making the misrepresentation and what was obtained or given up thereby.'" *Schaller Tel. Co.*, 298 F.3d at 746 (quoting *Bennett*, 685 F.2d at 1062). Conclusory allegations of fraud and deception are insufficient. *U.S. ex rel. Joshi v. St. Luke's Hosp., Inc.*, 441 F.3d 552, 556-57 (8th Cir. 2006); *see also Erdman Co. v. Phoenix Land & Acquisition, LLC*, No. 2:10-CV-2045, 2013 WL 3772675, at *2 (W.D. Ark. Jul. 17, 2013) ("Because the pleading standard is higher for fraud claims than for other claims, conclusory allegations are not enough to satisfy Rule 9(b).").

Where a complaint "fails to set forth the particular false representations of material fact that were allegedly made," it is subject to mandatory dismissal. *Anfield-El v. Wells Fargo Home Mortg.*, No. 5:15-CV-05165, 2015 WL 5547437, at *2 (W.D. Ark. Sept. 21, 2015). Such a fraud claim is insufficient, for example, where it does not identify

> (1) the particular individuals who are alleged to have . . . engaged in any of the other fraudulent practices alleged; (2) when any of the specific acts of alleged fraud occurred; (3) who was involved in the fraudulent [] aspect of the conspiracy; (4) what services were provided and to which patients the services were provided; (5) what the content was of the fraudulent claims; [or] (6) to which patients the medical equipment and services were provided . . . .

U.S. ex rel. Piacentile v. Beverly Enterprises, Inc., No. CIV. 04-5285, 2006 WL 686474, at *2 (W.D. Ark. Mar. 16, 2006); *see also Owen*, 2019 WL 2583519, at *2 (dismissing a fraud claim where the complaint failed to include "any allegations concerning who made the allegedly fraudulent statements, when or where the statements were made, or facts pertaining to the content of the statements").

Here, the Complaint does not identify (1) the particular Pfizer employees who are alleged to have "deliberately and intentionally misrepresented to, and omitted and/or concealed material facts from, consumers, including Plaintiffs"; (2) the specific date(s) any such "misrepresentation" was communicated to Plaintiffs; (3) the specific contents of any such misrepresentation, beyond vague allegations about the safety and efficacy of Xeljanz; or (4) how the allegedly fraudulent statements were communicated to Plaintiffs, be it orally or in writing. Instead, Plaintiffs allege, in conclusory fashion, that Pfizer "made misrepresentations of material facts to, omitted and/or concealed material facts from [Mrs. Stube's] prescribing physician and [Mrs. Stube] during the life cycle of the product," and that it "deliberately and intentionally misrepresented to, and omitted and/or concealed material facts from, consumers." Those allegations fail to pass muster under Rule 9(b). Without more particularity regarding the alleged

misrepresentations, Pfizer is unable to determine at this point what exactly Plaintiffs are alleging that it did to defraud them. Because Plaintiffs have failed to allege "the time, place and contents of false representations, as well as the identity of the person making the misrepresentation," the fraud claim is subject to dismissal.

III. Plaintiffs Fail to State a Claim for Negligent Misrepresentation.

"Cause V" of the Complaint includes allegations styled under the heading "negligent misrepresentation." Dkt. No. 2, ¶¶ 91–100. Here, Plaintiffs claim Pfizer "owed a duty to disseminate accurate and adequate information concerning Xeljanz, and to exercise reasonable care to ensure that it did not, in those undertakings, create unreasonable risks of personal injury to others." *Id.*, ¶ 93. They further allege Pfizer made "misrepresentations . . . in publications and other written materials directed to physicians (including Plaintiff[s'] prescribing physician), patients, and the general public with the intention of inducing reliance by Plaintiff[s'] prescribing physician and by Plaintiff[s]." *Id.*, ¶ 97.

Not only do Plaintiffs' negligent misrepresentation allegations fail to meet the heightened pleading standard set forth in Rule 9(b), *see Owen*, 2019 WL 2583519, at *2, the Court must dismiss the claim because Arkansas law does not recognize the tort of negligent misrepresentation. *S. Cty., Inc.*, 315 Ark. at 725; *see also Curtis Lumber Co. v. Louisiana Pac. Corp.*, 618 F.3d 762, 774 (8th Cir. 2010) ("The district court correctly stated that Arkansas does not recognize a tort of negligent misrepresentation . . . ."). Plaintiffs' claim for negligent misrepresentation is thus subject to dismissal under Rule 12(b)(6).

IV. Plaintiffs Fail to State a Claim for Gross Negligence.

Plaintiffs' final claim is one of "gross negligence." Dkt. No. 2, ¶¶ 101–106. In this portion of the Complaint, Plaintiffs repeat the same allegations of negligence against Pfizer, but

with less factual detail. *Compare id.*, ¶ 83 ("Defendant owed a duty to Plaintiff's prescribing physicians and Plaintiff to use reasonable care in testing, labeling, manufacturing, marketing, supplying, distributing and selling Xeljanz, including a duty to ensure that Xeljanz did not cause users to suffer from unreasonable, unknown, and dangerous side effects."), *and* ¶ 84 ("Defendant failed to exercise reasonable care and failed to warn of the known risks associated with the risks of Xeljanz. The product lacked sufficient warnings regarding the hazards and dangers to users of Xeljanz, and failed to provide safeguards to prevent the injuries sustained by Plaintiff. Defendant failed to properly test, analyze and report on the safety profile of Xeljanz prior to its sale, and as a result, subjected users to an unreasonable risk of injury when those products were used as directed."), *with id.*, ¶ 102 ("Defendant had the duty to exercise reasonable care in testing, manufacturing, marketing, labeling, selling, and/or distributing Xeljanz including a duty to ensure that Xeljanz did not cause users to suffer from unreasonable and dangerous side effects.") *and* ¶ 103 ("Defendant failed to exercise reasonable care in testing, manufacturing, marketing, labeling, selling, and/or distributing Xeljanz for the reasons set forth above.").

Rule 12(b)(6) requires the dismissal of the gross negligence claim. To state a claim for gross negligence, Plaintiffs must allege that Pfizer went well beyond merely negligent conduct and instead failed "to use even slight care." *IPSCO Tubulars, Inc.*, 779 F.3d at 752 (affirming the dismissal of gross negligence claim under Arkansas law). As such, the Complaint must include plausible allegations that "intentional[ly] fail[ed] to perform a manifest duty in reckless disregard of the consequences as affecting the life or property of another." *Key v. Coryell*, 86 Ark. App. 334, 346, 185 S.W.3d 98, 107 (2004). Nothing in the Complaint suggests that Pfizer acted in such a manner. Tellingly, Plaintiffs' allegations of gross negligence are confined to just five paragraphs. Dkt. No. 2, ¶¶ 102–106. And the allegations included in those paragraphs

mirror those directed toward Pfizer in the ordinary negligence portion of the Complaint. *See id.*, ¶¶ 82–90. Allegations which are indistinguishable from a claim for simple negligence do not evince "a failure to use even slight care." As a result, Plaintiffs' gross negligence claim is subject to dismissal.

V. Plaintiffs Fail to State a Claim for Punitive Damages.

The Complaint includes a request for punitive damages. *See id.* at 34 ("Prayer for Relief"). To support that plea for exemplary relief, Plaintiffs claim that "[Pfizer's] conduct in the testing, packaging, warning, marketing, advertising, promotion, distribution, and sale of Xeljanz was committed with knowing, conscious and deliberate disregard for the rights and safety of consumers such as Plaintiffs, thereby entitling Plaintiffs to punitive damages." *Id.*, ¶ 57. They also allege that Pfizer's "conduct in concealing material facts and making the foregoing misrepresentations, as alleged herein, was committed with conscious or reckless disregard of the rights and safety of consumers such as Plaintiffs" and that Pfizer acted "with knowing, conscious, and deliberate disregard for the rights and safety of consumers such as Plaintiffs." *Id.*, ¶¶ 73, 81. Similar conclusory allegations of recklessness are scattered in other portions of the Complaint. *See id.*, ¶¶ 90, 100, 106.

Arkansas law makes clear that Plaintiffs must clear a high bar before punitive damages may be awarded. Plaintiffs have failed to clear that threshold on the pleadings. In order to recover punitive damages, a plaintiff has the burden of proving that the defendant is liable for compensatory damages and that either or both of the following aggravating factors were present and related to the injury for which compensatory damages were awarded:

> (1) The defendant knew or ought to have known, in light of the surrounding circumstances, that his or her conduct would naturally and probably result in injury or damage and that he or she continued the conduct with malice or in reckless disregard of the consequences from which malice may be inferred; and

> (2) The defendant intentionally pursued a course of conduct for the purpose of causing injury or damage.

Ark. Code Ann. § 16-55-206. Pursuant to the statute, punitive damages are appropriate only "when evidence indicates that a person acted wantonly in causing injury or with such conscious indifference to the consequences that malice may be inferred." *Orsini v. Larry Moyer Trucking, Inc.*, 310 Ark. 179, 182, 833 S.W.2d 366, 368 (1992). "Gross dereliction of duty does not warrant punitive damages," *id.*, as there must be proof of intentional wrong or a conscious indifference to the consequences of one's actions. *See Welder v. Mercer*, 247 Ark. 999, 1003, 448 S.W.2d 952, 954 (1970). Malice is "'an intent and disposition to do a wrongful act gravely injurious to another.'" *Satterfield v. Rebsamen Ford, Inc.*, 253 Ark. 181, 186, 485 S.W.2d 192, 195 (1972) (quoting *Ray Dodge, Inc. v. Moore*, 251 Ark. 1036, 1042, 479 S.W.2d 518, 522 (1972)).

In addition, Plaintiffs must prove by "clear and convincing evidence" that Pfizer acted with malice, reckless disregard, or intent in order to obtain an award of punitive damages. *See* Ark. Code Ann. § 16-55-207. "Clear and convincing evidence" is "proof that produces a firm conviction in you that the allegation is true." *Carter v. Four Seasons Funding Corp.*, 351 Ark. 637, 653, 97 S.W.3d 387, 395 (2003). Punitive damages must be based on "the extent and enormity of the wrong, the intent of the party committing the wrong, all the circumstances, and the financial and social condition and standing of the erring party" because such damages are intended to penalize malicious conduct done deliberately to injure another. *See Edwards v. Stills*, 335 Ark. 470, 483-84; 984 S.W.2d 366, 373 (1998).

In this case, Plaintiffs have alleged no facts that, if true, would support a finding that Pfizer "knew or ought to have known . . . that [its] . . . conduct would naturally and probably

result in injury or damage and that [it] . . . continued the conduct with malice or in reckless disregard of the consequences." Likewise, Plaintiffs have not shown that Pfizer "intentionally pursued a course of conduct for the purpose of causing injury or damage." To the contrary, the Complaint demonstrates that Pfizer complied with its federal obligations and included the strongest warning permitted by FDA. Pfizer specifically warned Mrs. Stube prescribing physician that "**Patients treated with XELJANZ are at increased risk for developing serious infections that may lead to hospitalization or death."** Exhibit A, at 2 (emphasis in original). Similarly, Pfizer included a warning concerning the potentially life-threatening outcomes associated with serious infection. *See id.* at 1 ("**Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving XELJANZ**." (emphasis in original)).

The Complaint simply cannot overcome the strongly worded warnings found on the Xeljanz label, all of which were done at the direction, and with the consent, of FDA regulators. Absent allegations of something more, Plaintiffs' punitive damages claim arises from nothing other than their disagreement with Pfizer's obligations under federal law. That is insufficient under Arkansas law, where even gross negligence will not support an award of punitive damages. *See Nat'l By-Products, Inc.*, 292 Ark. at 494, 731 S.W.2d at 196. Because the Complaint lacks any allegations capable of sustaining an award of punitive damages, the Court should dismiss that claim with prejudice.

CONCLUSION

For the reasons stated above, Plaintiffs' Complaint should be dismissed in its entirety and with prejudice.

This 9th day of September, 2019.

Lyn P. Pruitt (Ark. Bar No. 84121)
Scott D. Provencher (Ark. Bar No. 96148)
Graham C. Talley (Ark. Bar No. 2015159)
MITCHELL, WILLIAMS, SELIG,
GATES & WOODYARD, P.L.L.C.
425 W. Capitol Ave., Suite 1800
Little Rock, AR 72201
Phone: 501-688-8800
Fax: 501-688-8807
lpruitt@mwlaw.com
sprovencher@mwlaw.com
gtalley@mwlaw.com

Attorneys for Defendant Pfizer Inc.